



Appl. No. 09/724,571
Amdt. dated November 7, 2003

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Amendments to the Specification:

Please replace the paragraph beginning on page 9, line 9 with the following amended paragraph:

FIG. 13(A-E) shows the nucleotide sequence of pCEK clone 27 (SEQ ID NO:48), with the ~~ORF~~ ORF indicated by the amino acid sequence SEQ ID NO:2.

Please replace the paragraph beginning on page 30, line 5 with the following amended paragraph:

The full-length open reading frame (ORF) of human β -secretase is described above, and its sequence is shown in FIG. 2A as SEQ ID NO: 2. However, as mentioned above, a further discovery of the present invention indicates that the predominant form of the active, naturally occurring molecule is truncated at the N-terminus by about 45 amino acids. That is, the protein purified from natural sources was N-terminal sequenced according to methods known in the art (Argo Bioanalytica, Morris Plains, NJ,). The N-terminus yielded the following sequence: EGDEEPEEPGRRGSFVEMVDNLRG... (SEQ ID NO: 55). This corresponds to amino acids 46-69 of the ORF-derived putative sequence. Based on this observation and others described below, the N-terminus of an active, naturally occurring, predominant human brain form of the enzyme is amino acid 46, with respect to SEQ ID NO: 2. Further processing of the purified protein provided the sequence of an internal peptide: IGFAVSACHVHDEFR ~~ISFAVSACHVHDEFR~~ (SEQ ID NO: 56), which is amino terminal to the putative transmembrane domain, as defined by the ORF. These peptides were used to validate and provide reading frame information for the isolated clones described elsewhere in this application.